

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number:

k093867

B. Purpose for Submission:

New device

C. Measurand:

Opiates

D. Type of Test:

Qualitative and semi-quantitative immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

DAT Oral Fluid Opiates (OFOPI)
Oral Fluid DAT Qual Cal A
Oral Fluid DAT SQ Cal A
Oral Fluid DAT Control Set A

G. Regulatory Information:

1. Regulation section:

862.3650, opiate test system
862.3200, clinical toxicology calibrator
862.3280, clinical toxicology control material

2. Classification:

Class II
Class II
Class I, reserved

3. Product Code:

DJG, enzyme immunoassay, opiates
DKB, calibrator, drug mixture
DIF, drug mixture control materials

4. Panel:

All are Toxicology (91)

H. Intended Use:

1. Intended use(s):

Refer to Indications for use.

2. Indication(s) for use

DAT Oral Fluid Opiates (OFOPi) is an in vitro diagnostic test for the qualitative and semiquantitative detection of opiates in human oral fluid at a cutoff concentration of 30 ng/mL in neat oral fluid. The specimen must be collected exclusively with the Intercept® Oral Specimen Collection Device. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program and to estimate a dilution of the specimen for confirmation by a confirmatory method such as LC/MS/MS.

DAT Oral Fluid Opiates provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Chromatography/mass spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

The Oral Fluid DAT Control Set A is for use as assayed controls with the DAT Oral Fluid assays on automated clinical chemistry analyzers for human oral fluid samples collected with the Intercept Oral Specimen Collection Device.

The Oral Fluid DAT Qual Cal calibrators are designed for the calibration of oral fluid assays for drugs of abuse on automated clinical chemistry analyzers for human oral fluid samples collected with the Intercept Oral Specimen Collection Device.

The Oral Fluid DAT SQ Cal A calibrators are designed for the calibration of oral fluid assays for drugs of abuse on automated clinical chemistry analyzers for human oral fluid samples collected with the Intercept Oral Specimen Collection Device.

3. Special condition for use statement(s)

For prescription use only.

The assay is not designated for use in point-of-care settings.

Tests for opiates cannot distinguish between abused drugs and certain prescribed medications.

Certain foods or medications may interfere with tests for opiates and cause false positive results.

4. Special instrument Requirements:

Roche Modular P analyzer.

I. Device Description:

The Oral Fluid Opiates assay consists of two ready for use reagent solutions, calibrators, and controls. Calibrators and controls are prepared by the quantitative addition of analyte to a synthetic oral fluid matrix. Calibrators and controls are required but not supplied with the reagents.

Reagent 1 (R1) contains antibody/microparticle working solution with microparticles attached to morphine antibody (mouse monoclonal) in buffer with bovine serum albumin (BSA) and 0.09% sodium azide.

Reagent 2 (R2) contains conjugate working solution with conjugated morphine derivative in buffer with bovine serum albumin (BSA) and 0.09% sodium azide.

Calibrators: *Qualitative* assay required calibrator: CAL 2 (10 ng/mL)

Semiquantitative assay required calibrators: CAL 0 (0 ng/mL), CAL 1 (5 ng/mL), CAL 2 (10 ng/mL), CAL 3 (20 ng/mL), CAL 4 (40 ng/mL), CAL 5 (80 ng/mL)

Controls: Zero, Negative (0.5X), and Positive (1.5X)

J. Substantial Equivalence Information:

1. Predicate device name:

STC Technologies, STC Opiates Intercept Micro-Plate EIA

2. Predicate k number:

k981341

3. Comparison with predicate:

| Similarities | | |
|---------------------------|--|---|
| Item | Device | Predicate |
| Indications for Use | Same | For use in the determination of opiates in oral fluid collected with the Intercept Drugs of Abuse (DOA) Oral Specimen Collection Device. For In Vitro Diagnostic Use. |
| Methodology | Same | Immunoassay |
| Differences | | |
| Item | Device | Predicate |
| Cutoff | 30 ng/mL in Neat Oral Fluid | 10 ng/mL when oral fluid collected with the Oral Specimen Collection Device |
| Platform | Roche Modular P analyzer | Microplate |
| Control concentrations | Synthetic oral fluid matrix: Zero, Negative (.5X), and Positive (1.5X) | Negative (.5X) and Positive (2X) |
| Calibrator concentrations | Zero, .5X, Cutoff, 2X, 4X, and 8X | Zero, Cutoff |
| Measurement mode | Qualitative and semi-quantitative measurements | Qualitative measurements only |

K. Standard/Guidance Document Referenced (if applicable):

The sponsor referenced the following standard in their submission:

- CLSI EP5-A2 Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline - 2nd edition

The sponsor referenced the following guidance document(s) in their submission:

- Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests - Draft Guidance for Industry and FDA Staff

L. Test Principle:

The assay is based on the kinetic interaction of microparticles in a solution (KIMS) as measured by changes in light transmission. In the absence of sample drug, soluble drug conjugates bind to antibody-bound microparticles, causing the formation of particle aggregates. As the aggregation reaction proceeds in the absence of sample drug, the absorbance increases. When an oral fluid sample contains the drug in question, this drug competes with the drug derivative conjugate for microparticle-bound antibody. Antibody bound to sample drug is no longer available to promote particle aggregation, and subsequent particle lattice formation is inhibited. The presence of sample drug diminishes the increasing absorbance in proportion to the concentration of drug in the sample.

The Intercept® Oral Specimen Collection Device contains a preservative buffer that dilutes the neat oral fluid sample. The calibrator and control levels are set at diluted levels so that sample absorbance values can be compared directly to the absorbance values of the calibration curve. The assay result is reported as a positive or negative result relative to the neat oral fluid cutoff of 30 ng/mL.

NOTE: To correlate a semi-quantitative result from the assay or the associated LC/MS/MS confirmation result to a neat oral fluid value, the result from the assay or the associated LC/MS/MS confirmation test should be multiplied by a factor of 3.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All analytical performance data was collected on human oral fluid samples collected with the Intercept Oral Specimen Collection Device and analyzed on the Roche MODULAR P analyzer. The Intercept collection device includes a diluent that results in a dilution of approximately 1/3. The assay cannot be used to measure undiluted (neat) samples. Analyte concentrations refer to the neat oral fluid concentration, unless otherwise noted.

a. Precision/Reproducibility:

Two studies were performed with the assay to evaluate precision.

In the first study, a morphine solution was added to each of 9 samples which were obtained from a human oral fluid pool of samples collected with the Intercept® Oral Specimen Collection Device. The resulting concentrations were approximately -100 %, -

75 %, -50 %, -25 %, 0 %, +25 %, +50 %, +75 %, and +100 % of the cutoff calibrator value. The samples were tested in qualitative and semiquantitative modes. Following a CLSI (EP5-A2) precision protocol, samples were tested in 2 replicates per run, 2 runs per day for 21 days, total n = 84. One lot each of reagent, calibrator, and control were used and there were 19 calibrations performed during the study.

Qualitative Mode

Note: this study was performed on samples already collected with the Intercept collection device. Therefore the data in the table below do not reflect any imprecision inherent in the collection process itself. Results were as follows:

| Drug | Concentration of Sample, ng/mL | Number of Determinations | Results #Neg / #Pos |
|----------|--------------------------------|--------------------------|---------------------|
| Morphine | zero drug | 84 | 84 Neg / 0 Pos |
| Morphine | -75% | 84 | 84 Neg / 0 Pos |
| Morphine | -50% | 84 | 84 Neg / 0 Pos |
| Morphine | -25% | 84 | 84 Neg / 0 Pos |
| Morphine | cutoff | 84 | 52 Neg / 32 Pos |
| Morphine | +25% | 84 | 0 Neg / 84 Pos |
| Morphine | +50% | 84 | 0 Neg / 84 Pos |
| Morphine | +75% | 84 | 0 Neg / 84 Pos |
| Morphine | +100% | 84 | 0 Neg / 84 Pos |

Semiquantitative Mode

Note: this study was performed on samples already collected with the Intercept collection device. Therefore the data in the table below do not reflect any imprecision inherent in the collection process itself. Results were as follows:

| Drug | Conc. of Sample, ng/mL | Results #Neg / #Pos | Within-run Precision | | Total Precision | |
|----------|------------------------|---------------------|----------------------|------|-----------------|------|
| | | | SD ng/mL | CV % | SD ng/mL | CV % |
| Morphine | zero drug | 84 Neg / 0 Pos | 0.31 | 40.1 | 0.35 | 45.1 |
| Morphine | -75% | 84 Neg / 0 Pos | 0.27 | 11.4 | 0.31 | 13.3 |

| Drug | Conc. of Sample, ng/mL | Results #Neg / #Pos | Within-run Precision | | Total Precision | |
|----------|------------------------|---------------------|----------------------|-----|-----------------|-----|
| | | | | | | |
| Morphine | -50% | 84 Neg / 0 Pos | 0.24 | 5.3 | 0.34 | 7.4 |
| Morphine | -25% | 84 Neg / 0 Pos | 0.30 | 4.6 | 0.36 | 5.4 |
| Morphine | cutoff | 47 Neg / 37 Pos | 0.35 | 3.5 | 0.46 | 4.7 |
| Morphine | +25% | 0 Neg / 84 Pos | 0.39 | 3.1 | 0.49 | 3.9 |
| Morphine | +50% | 0 Neg / 84 Pos | 0.39 | 2.7 | 0.46 | 3.2 |
| Morphine | +75% | 0 Neg / 84 Pos | 0.36 | 2.1 | 0.48 | 2.9 |
| Morphine | +100% | 0 Neg / 84 Pos | 0.49 | 2.5 | 0.56 | 2.9 |

In the **second** study, a morphine solution was added to neat human oral fluid sample pools at concentrations of 15, 22.5, 37.5, and 45 ng/mL. Each sample was then processed through each of 21 of the Intercept® Oral Specimen Collection Devices to achieve final concentrations at approximately -50 %, -25 %, +25 %, and +50 % of the cutoff calibrator value. The intra-assay precision of the samples, including the processing of the samples through the collection device, was then tested in qualitative and semiquantitative modes with the Oral Fluid Opiates assay.

Qualitative Mode

Note: The values obtained in this study were collected from samples spiked with morphine prior to the collection step. Therefore the data in the table below reflects the performance of the entire system including the collection step.

| Drug | Concentration of Sample | Number of Determinations | Results #Neg / #Pos |
|----------|-------------------------|--------------------------|---------------------|
| Morphine | -50% | 21 | 21 Neg / 0 Pos |
| Morphine | -25% | 21 | 18 Neg / 3 Pos |
| Morphine | +25% | 21 | 0 Neg / 21 Pos |
| Morphine | +50% | 21 | 0 Neg / 21 Pos |

Semiquantitative Mode

Note: The values obtained in this study were collected from samples spiked with morphine prior to the collection step. Therefore the data in the table below reflects the performance of the entire system including the collection step.

| Drug | Conc. of Sample | Results #Neg / #Pos | Precision | |
|----------|-----------------|------------------------|-----------|------|
| | | | SD ng/mL | CV % |
| Morphine | -50% | 21 Neg / 0 Pos | 0.57 | 7.8 |
| Morphine | -25% | 14 Neg / 7 Pos | 0.55 | 5.6 |
| Morphine | +25% | 0 Neg / 21 Pos | 0.57 | 3.8 |
| Morphine | +50% | 0 Neg / 21 Pos | 0.55 | 3.0 |

b. Linearity/assay reportable range:

To assess linearity, aliquots of a neat OF pool were spiked with morphine at concentrations of 0, 15, 22.5, 30, 37.5, 45, 60, 120, and 240 ng/mL. Each level was processed through 2 separate Intercept collection devices. The diluted sample from both Intercept devices was then analyzed once in semi-quantitative mode. The data below was analyzed with one calibration using one lot of reagent.

Results were as follows:

| Spiked Neat Concentration | Recovery (%) |
|---------------------------|--------------|
| 0 | n/a |
| 15 | 92.6 |
| 22.5 | 96.9 |
| 30 (cutoff) | 98.0 |
| 37.5 | 95.0 |
| 45 | 101.5 |
| 60 | 100.0 |
| 120 | 97.1 |
| 240 | 101.6 |

c. Traceability (controls, calibrators, or method):

The assay is calibrated against morphine.

Calibrators and control materials are specified in the labeling but are supplied separately from the reagents. For the qualitative assay, only CAL 2 (10 ng/mL) is required. For the semi-quantitative assay, six levels of calibrator material, ranging in concentration from 0 to 80 ng/mL are required. Calibrators and controls consist of a synthetic oral fluid matrix spiked with known concentrations of morphine.

The concentration of morphine in the calibrators and controls is verified by LC/MS/MS.

The open vial stability claim for calibrators and controls is 20 days after opening when stored at 2–8° C. The closed vial stability claim for calibrators and controls is one year from the time of manufacture when stored at 2–8° C.

The sponsor's stability protocols were reviewed and found to be acceptable.

d. Detection limit:

Performance at low drug concentrations in the semi-quantitative assay was characterized by determination of recovery (see section b above).

e. Analytical specificity:

The sponsor performed analytical specificity studies on four categories of potential interferents: structurally related substances, structurally unrelated substances, substances endogenous to oral fluid, and food and dental substances.

Cross Reactivity to Structurally Related Compounds

Cross-reactivity was evaluated by spiking various concentrations of similarly structured drug compounds into a drug-free oral fluid pool collected with the Intercept Oral Fluid Specimen Collection Device. By analyzing various concentration of each compound the sponsor determined the concentration of the drug that produced a response approximately equivalent to the cutoff concentration of the assay. Results of those studies appear in the table below:

| Drug compound | Approximate Percent Cross-reactivity |
|--------------------------|--------------------------------------|
| Ethylmorphine | 182 |
| Codeine | 147 |
| Heroin | 100 |
| 6-monoacetylmorphine | 83 |
| Dihydrocodeine | 62 |
| Morphine-3-β-glucuronide | 48 |

| Drug compound | Approximate Percent Cross-reactivity |
|------------------|--------------------------------------|
| Thebaine | 30 |
| Hydrocodone | 26 |
| Hydromorphone | 19 |
| Nalorphine | 11 |
| Rifampin | 9 |
| Levorphanol | 6 |
| Oxymorphone | 0.28 |
| Oxycodone | 0.26 |
| Meperidine | 0.24 |
| Buprenorphine | 0.18 |
| Normorphine | 0.16 |
| Naloxone | 0.08 |
| Dextromethorphan | 0.04 |
| Naltrexone | 0.03 |

Interference from Structurally Unrelated Compounds

Potential interference from structurally unrelated compounds was tested in both semi-quantitative and qualitative mode by spiking the potentially interfering compound into pools of human oral fluid collected with the Intercept Oral Fluid Specimen Collection Device. Both a positive concentration (+50% of the cutoff) and a negative concentration (-50% of the cutoff) of morphine were evaluated. All were tested at a concentration of 10,000 ng/mL with the following exceptions:

Trifluoperazine – tested at 3,000 ng/mL

Atropine – tested at 5,000 ng/mL

Trimipramine – tested at 5,000 ng/mL

| Generic Name | Tested Concentration (ng/mL) | Approximate Neat Concentration (ng/mL) |
|-----------------------|------------------------------|--|
| 4-Aminophenyl sulfone | 10,000 | 30,000 |
| Acetaminophen | 10,000 | 30,000 |
| Acetylsalicylic acid | 10,000 | 30,000 |
| Alprazolam | 10,000 | 30,000 |

| Generic Name | Tested Concentration (ng/mL) | Approximate Neat Concentration (ng/mL) |
|---------------------|-------------------------------------|---|
| Amitriptyline | 10,000 | 30,000 |
| Amobarbital | 10,000 | 30,000 |
| d-Amphetamine | 10,000 | 30,000 |
| l-Amphetamine | 10,000 | 30,000 |
| Ampicillin | 10,000 | 30,000 |
| Aspartame | 10,000 | 30,000 |
| Atropine | 5,000 | 15,000 |
| Benzococaine | 10,000 | 30,000 |
| Benzoylcegonine | 10,000 | 30,000 |
| Buprenorphine | 10,000 | 30,000 |
| Butabarbital | 10,000 | 30,000 |
| Caffeine | 10,000 | 30,000 |
| Chlordiazepoxide | 10,000 | 30,000 |
| Cocaine | 10,000 | 30,000 |
| Cotinine | 10,000 | 30,000 |
| Cyclizine | 10,000 | 30,000 |
| Desipramine | 10,000 | 30,000 |
| Diazepam | 10,000 | 30,000 |
| Diphenhydramine | 10,000 | 30,000 |
| Doxepin | 10,000 | 30,000 |
| d-ephedrine | 10,000 | 30,000 |
| l-ephedrine | 10,000 | 30,000 |
| d,l-ephedrine | 10,000 | 30,000 |
| Fenoprofen | 10,000 | 30,000 |
| Fluoxetine | 10,000 | 30,000 |
| Gentisic acid | 10,000 | 30,000 |
| Glipizide | 10,000 | 30,000 |
| Ibuprofen | 10,000 | 30,000 |
| Imipramine | 10,000 | 30,000 |
| Ketamine | 10,000 | 30,000 |
| Loperamide | 10,000 | 30,000 |
| LSD | 10,000 | 30,000 |

| Generic Name | Tested Concentration (ng/mL) | Approximate Neat Concentration (ng/mL) |
|---------------------|-------------------------------------|---|
| MDMA | 10,000 | 30,000 |
| Methadone | 10,000 | 30,000 |
| d-Methamphetamine | 10,000 | 30,000 |
| l-Methamphetamine | 10,000 | 30,000 |
| Methaqualone | 10,000 | 30,000 |
| Naproxen | 10,000 | 30,000 |
| Niacinamide | 10,000 | 30,000 |
| Nicotine | 10,000 | 30,000 |
| Nordiazepam | 10,000 | 30,000 |
| Oxazepam | 10,000 | 30,000 |
| Pantoprazole | 10,000 | 30,000 |
| Penicillin G | 10,000 | 30,000 |
| Pentazocine | 10,000 | 30,000 |
| Pentobarbital | 10,000 | 30,000 |
| Phencyclidine | 10,000 | 30,000 |
| Phenobarbital | 10,000 | 30,000 |
| Phenylephrine | 10,000 | 30,000 |
| Phenylpropanolamine | 10,000 | 30,000 |
| Procainamide | 10,000 | 30,000 |
| Procaine | 10,000 | 30,000 |
| Promethazine | 10,000 | 30,000 |
| Pseudoephedrine | 10,000 | 30,000 |
| Quetiapine | 10,000 | 30,000 |
| Quinidine | 10,000 | 30,000 |
| Ranitidine | 10,000 | 30,000 |
| Secobarbital | 10,000 | 30,000 |
| Δ 9-THC | 10,000 | 30,000 |
| Tramadol | 10,000 | 30,000 |
| Trifluoperazine | 3,000 | 9,000 |
| Trimipramine | 5,000 | 15,000 |
| Venlafaxine | 10,000 | 30,000 |

| Generic Name | Tested Concentration (ng/mL) | Approximate Neat Concentration (ng/mL) |
|---------------------|-------------------------------------|---|
| Zomepirac | 10,000 | 30,000 |

No negative or positive interference was seen in this study.

Interference from Endogenous Interferents and pH

Potential interference from substances endogenous to oral fluid were tested in both semi-quantitative and qualitative mode by spiking the potentially interfering substance into pools of human oral fluid collected with the Intercept Oral Fluid Specimen Collection Device. Both a positive concentration (+50% of the cutoff) and a negative concentration (-50% of the cutoff) of morphine were evaluated.

The following potential endogenous interferents were spiked into the negative and positive oral fluid samples at the noted concentrations. No negative or positive interference was seen in this study and all negative and positive controls recovered properly in the presence of the interfering substance in both qualitative and semi-quantitative modes.

| Interferent | Final Concentration |
|----------------------------|----------------------------|
| Albumin | 5 mg/mL |
| Salivary α -Amylase | 833 U/mL |
| Ascorbic Acid | 10 mg/mL |
| Bilirubin | 50 μ g/mL |
| Hemoglobin | 1 mg/mL |
| IgA | 0.33 mg/mL |
| IgG | 0.17 mg/mL |
| IgM | 0.033 mg/mL |

An additional study was performed in which samples containing morphine at +50% and -50% of the cutoff with pH ranging from 2.0 to 8.5 were tested. All of the samples above the cutoff read positive and all of the samples below the cutoff read negative.

Interference from Food and Dental Products

The following potential interferents were evaluated by spiking into oral fluid samples collected with the intercept device: alcohol (ethanol), antiseptic mouthwash, baking soda, cough syrup, whole blood, cranberry juice, hemoglobin, hydrogen peroxide, sodium chloride, sugar, toothpaste, and water. None of these substances caused positive or negative interference.

The effect of potential food and other oral cavity contaminants (alcohol, antacid, baking soda, chewing tobacco, cigarettes, cola, cough syrup, cranberry juice, gum, hard candy, milk, orange juice, salt, sugar, toothpaste, water, and tooth whitening strips) were also examined. No interference was observed in samples collected at least 10 minutes after the use of the above substances.

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision above.

2. Comparison studies:

a. Method comparison with predicate device:

Two method comparison studies were performed. In the first study, 20 positive and 20 negative samples were analyzed. In order to evaluate the performance of the entire system, three measurements were taken on each specimen: the LC/MS/MS concentration of the neat sample, the LC/MS/MS concentration of the diluted Intercept sample, and the immunoassay concentration of the diluted Intercept sample.

Sample description: clinical oral fluid samples

Number of study sites: one

Description of the site: manufacturer's facility

Type of study site: manufacturer's staff

Operator description: manufacturer's staff

Number of instruments used: one

The LC/MS/MS values of the neat and diluted samples confirmed the dilution ratio of approximately 1/3. When the LC/MS/MS values of the neat oral fluid samples were compared to the immunoassay

values, the following results were obtained. Note: The values obtained in this study were collected from samples containing opiates prior to the collection step. Therefore the results reflect the performance of the entire system including the collection step.

| Semi-Quantitative Mode | | | | |
|-------------------------------|---------------------------------------|--|--|---|
| | Low Neg by LC/MS/MS (less than - 50%) | Near Cutoff Negative by LC/MS/MS (Between -50% and cutoff) | Near Cutoff Positive by LC/MS/MS (Between cutoff and +50%) | High Positive by LC/MS/MS (greater than +50%) |
| Positive | 0 | 1* | 2 | 18 |
| Negative | 18 | 1 | 0 | 0 |

*Below are the opiate concentrations in neat oral fluid:

| Morphine (ng/mL) | Codeine (ng/mL) | 6-MAM (ng/mL) |
|------------------|-----------------|---------------|
| 22.8 | 0 | 0 |

LC/MS/MS values used to categorize samples in this table are based on the concentration of morphine, codeine, and 6 - monoacetylmorphine (6-MAM) found in the sample.

% Agreement among positives is 100%

% Agreement among negatives is 95%

| Qualitative Mode | | | | |
|-------------------------|---------------------------------------|---|--|---|
| | Low Neg by LC/MS/MS (less than - 50%) | Near Cutoff Negative by LC/MS/MS (Between - 50% and cutoff) | Near Cutoff Positive by LC/MS/MS (Between cutoff and +50%) | High Positive by LC/MS/MS (greater than +50%) |
| Positive | 0 | *2 | 2 | 18 |
| Negative | 18 | 0 | 0 | 0 |

*Below are the opiate concentrations in neat oral fluid:

| Morphine (ng/mL) | Codeine (ng/mL) | 6-MAM (ng/mL) |
|------------------|-----------------|---------------|
| 20.4 | 0 | 2.2 |
| 22.8 | 0 | 0 |

LC/MS/MS values used to categorize samples in this table are based on the concentration of morphine, codeine, and 6-monoacetylmorphine (6-MAM) found in the sample.

% Agreement among positives is 100%

% Agreement among negatives is 90%

In the second study, 40 negative and 40 positive samples were analyzed. These included four near cutoff negative samples and four near cutoff positive samples.

Note: this study was performed on samples already collected with the Intercept collection device. When the LC/MS/MS values of the diluted samples were compared to the immunoassay values, the following results were obtained. Therefore the results below do not reflect any inaccuracy inherent in the collection process itself.

| Semi-Quantitative Mode | | | | |
|-------------------------------|--------------------------------------|--|--|---|
| | Low Neg by LC/MS/MS (less than -50%) | Near Cutoff Negative by LC/MS/MS (Between -50% and cutoff) | Near Cutoff Positive by LC/MS/MS (Between cutoff and +50%) | High Positive by LC/MS/MS (greater than +50%) |
| Positive | 0 | 2* | 3 | 36 |
| Negative | 36 | 2 | 1# | 0 |

Below are the approximate opiate concentrations in neat oral fluid:

| | Morphine (ng/mL) | Codeine (ng/mL) | 6-MAM (ng/mL) |
|-----------|------------------|-----------------|---------------|
| *Sample 1 | 17.7 | 1.2 | 7.5 |
| *Sample 2 | 22.5 | 0 | 0 |
| #Sample 3 | 19.2 | 6.3 | 5.7 |

LC/MS/MS values used to categorize samples in this table are based on the concentration of morphine, codeine, and 6-monoacetylmorphine (6-MAM) found in the sample.

% Agreement among positives is 98%

% Agreement among negatives is 95%

| Qualitative Mode | | | | |
|-------------------------|---------------------------------------|---|--|---|
| | Low Neg by LC/MS/MS (less than - 50%) | Near Cutoff Negative by LC/MS/MS (Between - 50% and cutoff) | Near Cutoff Positive by LC/MS/MS (Between cutoff and +50%) | High Positive by LC/MS/MS (greater than +50%) |
| Positive | 0 | 2* | 4 | 36 |
| Negative | 36 | 2 | 0 | 0 |

Below are the approximate opiate concentrations in neat oral fluid:

| Morphine (ng/mL) | Codeine (ng/mL) | 6-MAM (ng/mL) |
|------------------|-----------------|---------------|
| 17.7 | 1.2 | 7.5 |
| 22.5 | 0 | 0 |

LC/MS/MS values used to categorize samples in this table are based on the concentration of morphine, codeine, and 6-monoacetylmorphine (6-MAM) found in the sample.

% Agreement among positives is 100%

% Agreement among negatives is 95%

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a and b are not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.